US Dept of Energy
Low Dose Radiation Research Program:

The Application of Genome Data to the Important Problem of Risk from Low Dose Radiation Exposure

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Presentation Goals

- Review the Low Dose Program
- Suggest ways the Genome Program may continue to contribute to the understanding of risk from low doses of radiation.

Problems Associated with Estimating Health Risks of Radiation

- Background radiation
- Background cancer
- Radiation is a poor Carcinogen

Normal annual exposure from natural radiation

300 mrem/yr


Radon gas	200 mrem
Human body	40 mrem
Rocks, soil	28 mrem
Cosmic rays	27 mrem

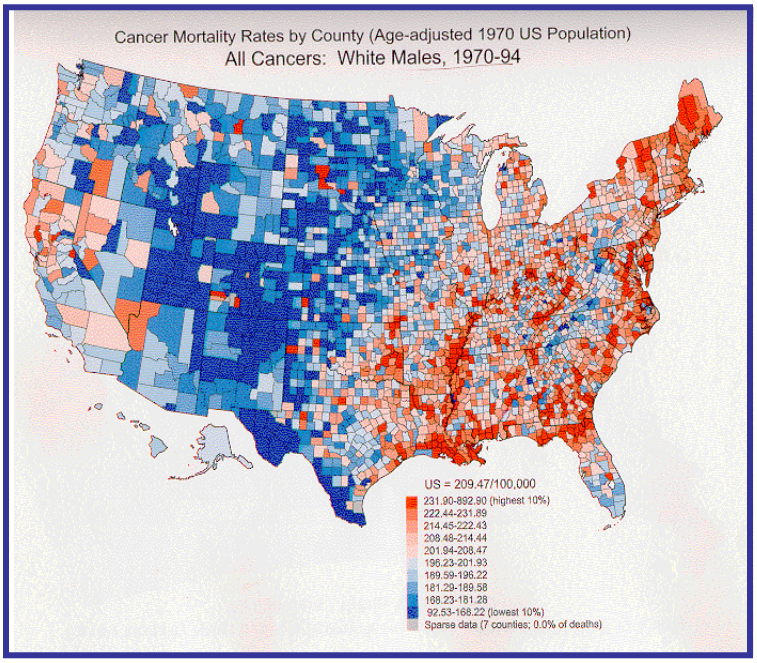

Normal annual exposure from man-made radiation

70 mrem/yr

Medical procedures	53 mrems
Consumer products	10 mrems
One coast to coast airplane flight	2 mrems
Watching color TV	1 mrem
Sleeping with another person	1 mrem
Weapons test fallout	less that 1 mrem
Nuclear industry	less than 1 mrem

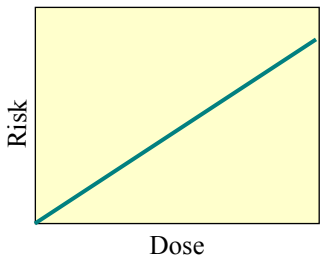




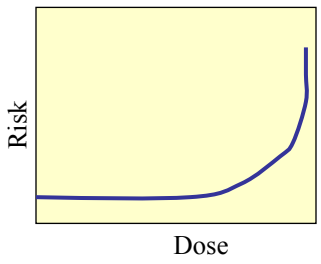


Risk Models

Linear No Threshold



Non-Linear Threshold



Is risk always proportional to dose?

Can any amount dose increase risk?

Can a single radioactive ionization can cause cancer?

Why now?

- Standards have been set from high dose effects, but low dose effects have not been measurable until now
- New technological developments and biological discoveries have made it possible to study low dose effects

DOE Low-Dose Radiation Research Program

- A 10 year program
- Focused on biological mechanisms of low-dose (< 0.1 Gy) and low dose-rate (< 0.1 Gy / Yr) radiation
- International in scope (currently 49 projects)
- To develop radiation standards based on risk
- We are interested in your ideas or proposals

http://lowdose.org

Key Research Areas

- Technological Advances
- Biological Advances

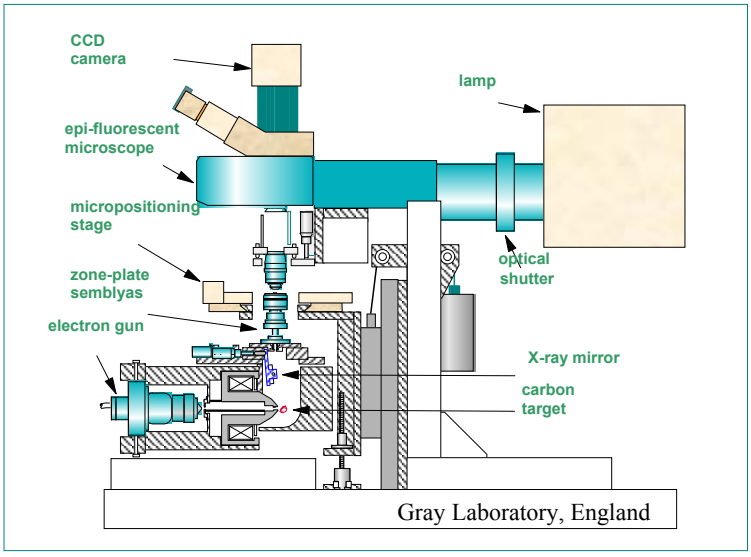
Regulation of Gene Expression

- DNA Damage and Repair
- Bystander Effect
- Adaptive Response

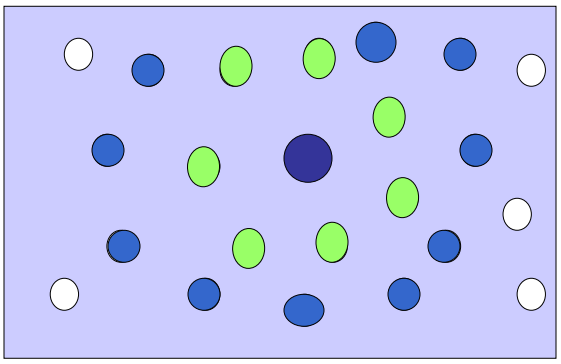
Rapid Sequence Information

- Genetic Susceptibility
- Characterize Mutations
- Generation of Transgenic Animals

Microbeam

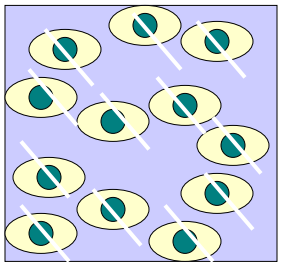


Bystander Effects

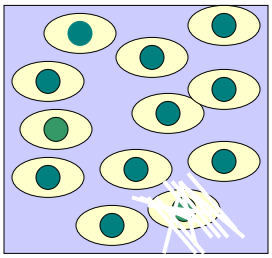


Microbeam

Each cell hit by one particle

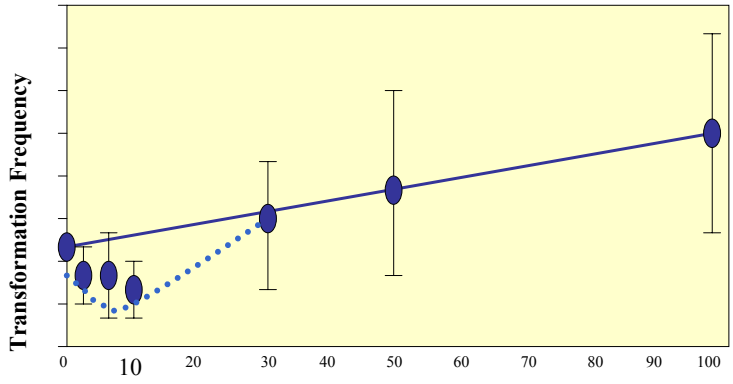


10 % of cells hit with 10 alpha particles



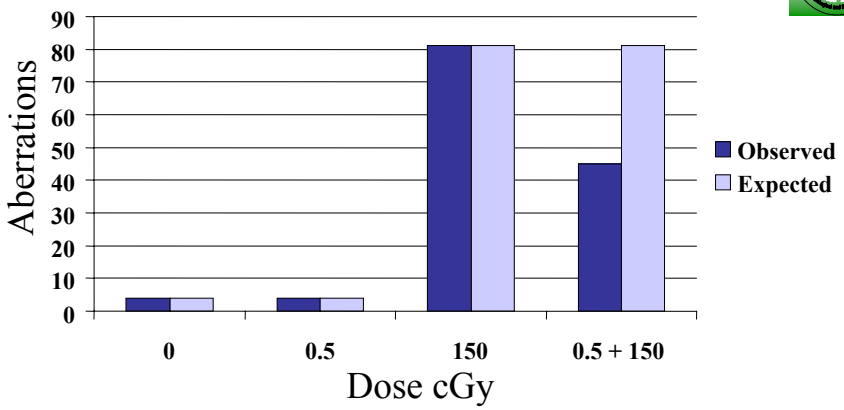
Hall

What Genes are Activated at Low Dose to Reduce Cell Transformation?



Redpath et al. 2001

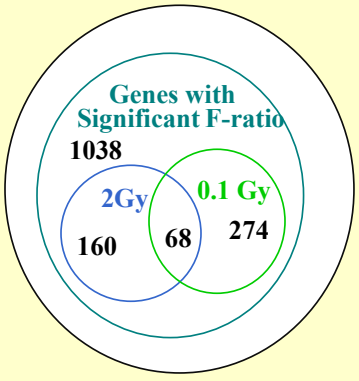
What Genes are Responsible for the Adaptive Response ?



Shadley and Wolff 1987

DIFFERENCES IN TRANSCRIPTION PROFILES BETWEEN LOW AND HIGH DOSE IRRADIATION IN HUMAN LYMPHOBLASTOID CELLS

HLB Cell Line



Total gene set contains over 12,000 genes

Numbers of Genes Differentially Regulated in HLB Cells after IR

Up-regulated at 2Gy	71
Down-regulated at 2Gy	147
Up-regulated at 0.1Gy	191
Down-regulated at 0.1Gy	141

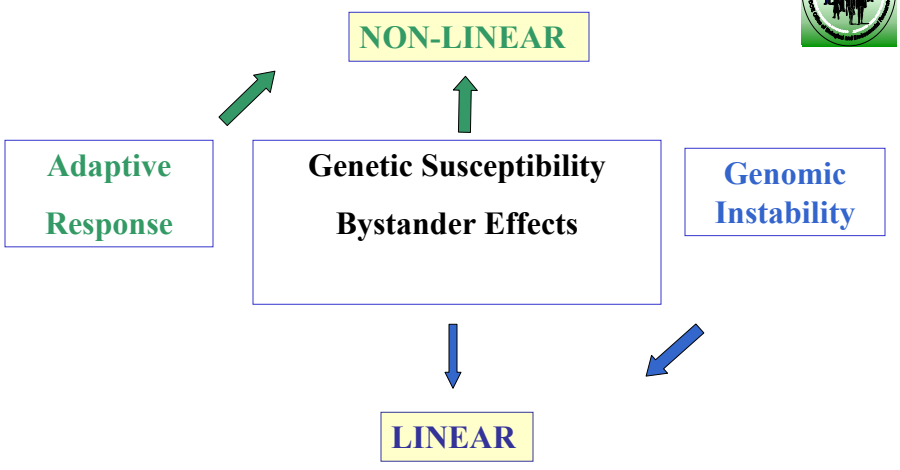
Wyrobek

Genetic Susceptibility

Who is susceptible to radiation?

Rapid gene sequencing makes identification possible.

How will this Research Impact the Shape of the Dose Response Curve?



Summary

- Scientific advances in the genome program have made it possible to focus on mechanisms of response to low dose radiation.
- The genome program provides scientific basis for radiation standards that are appropriate and adequate.
- Additional advances are necessary to understand and quantify low dose radiation risk.